[Supplementary online-only material for Mackay, Buckingham, Schwartz, et al.: The effect of biofeedback as a psychological intervention in multiple sclerosis: a randomized controlled study. *Int J MS Care.* 2015;17(3):101–108.]

Supplementary Appendix 1. **Flight/fight information**

The following script was read to participants:

"Your autonomic nervous system is the process that controls your automatic responses to threat. For example, if a grizzly bear was to appear at the door right now, both of us would have an automatic response generated by our autonomic nervous system. Adrenaline causes heart rate to increase, breathing to become rapid, and we would want to escape. Essentially, these responses occur because our brains respond this way to threat, to help us survive. Ideally, our bodies recover from stressful events by noting that the danger has passed, and returning our levels of adrenaline to normal. Breathing and muscle tension returns to normal. Even though our average day does not contain grizzly bears, many events occur that our brains respond to as a threat. An example may be when you are running late for an appointment and you notice your palms begin to sweat or your shoulders become tense. Unfortunately, in a day when many stressful events may have occurred, and there has been little or no chance to recover back to a normal breathing rate, a person may find themselves in a heightened state of arousal. This may lead to a chronically fast breathing rate, perpetually sore muscles, and a range of symptoms, from anxiety disorders to stomach upsets, headaches, and feeling that life is out of control.

Our aim today is to identify your current breathing rate and muscle tension, then to work on bringing these measures to within a relaxed state, effectively allowing your body's stress levels to return to normal."

Supplementary Appendix 2. **Biofeedback and questionnaire measures of assessment**

Biofeedback Measures

Thought Comp Infiniti hardware equipment was used, with Biograph Infiniti version 3.1.6 SA7900, 2003-2007 physiology suite software. Windows 97-2003 operating platform supported the software.

Quantitative Biofeedback measures comprising surface electromyography (EMG) and abdominal respiratory band (amplitude) biofeedback were used. These involve noninvasive sticky pad electrode placement on trapezius muscle (left and right shoulder, and an earth on the spine), and a respiratory band recording rate and amplitude of breath placed around the waist.

EMG in biofeedback measures an electrical correlate of muscle contraction and reads out in electrical units (μV).[22] Surface electrodes discs attach by a wire to the biofeedback machine, and the disc clips onto a small sticky square pad that adheres to the skin. The skin was prepared using an antiseptic swipe to remove dead skin cells and oils, and the sticky pad placed directly onto the large shoulder portion of the trapezius.

Biofeedback Breathing Recording

The biofeedback intervention comprised psychoeducation about the autonomic response, progressive muscle relaxation, a mindful breathing exercise, and training in diaphragmatic breathing, while biofeedback equipment (ThoughtTechnology Ltd, Version 3.1.6, 2003-2007, BioGraph Infiniti software) recorded breathing rate and trapezius muscle tension. A respiratory monitor was placed around the waist to record diaphragmatic movement and breathing rate in breaths per minute (bpm). An effective reduction in breathing rate was defined as ≥3 bpm

reduction from baseline. All participants viewed a computer screen graph that displayed waveforms corresponding to their in/out breath. Slowing down the breathing rate changed the visual display, and a "reward" was built into the program, which reinforced the desired behavior and increased learning (so that when breathing was at a relaxed rate, a picture of a spinning windmill appeared).

Biofeedback Muscle Tension Recording

Trapezius muscle activity was recorded by surface electrode placement on the trapezius at the belly of the shoulder portion of the muscle. During a relaxed state, trapezius muscle activity is typically less than 4 μV amplitude.[19] Participants visualized their muscle activity (as a green line graph) on a computer screen. They were taught how to associate the sensation of increased trapezius muscle activity with the amplitude displayed on the screen and adjust their muscle activity in order to reduce the overall reading. Hence, the EMG graphs served to immediately and visually reflect the physiological response, and internal awareness of that process was quickly gained, leading to self-regulation.

Questionnaires

The Coping Inventory for Stressful Situations (CISS)

The Coping Inventory for Stressful Situations (CISS)[22] is a 36-item self-report questionnaire. The authors of the CISS describe emotional-oriented coping as the use of coping efforts to reduce stress that are not always successful, such as worry and self-blame.[39] In turn, emotional-oriented coping has been correlated strongly with depression (as measured by the Beck Depression Inventory) and neuroticism (as measured by the STAI-S).

Internal consistency for the CISS measured by Cronbach alpha coefficients ranges from 0.87 for female adults to 0.92 for early male adolescents on the Task scale. On the Avoidance scale, alphas range from 0.85 for male undergraduates to 0.76 for female psychiatric patients. The Emotion scale alphas range from 0.82 for male psychiatric patients to 0.90 for adult males. Task and Emotion scales had good test-retest reliability above or equal to 0.68 for males and females. Avoidance scales had moderate retest reliability ranging from 0.51 to 0.60.[39] The CISS also has good external validity in clinically depressed populations. For the present study, internal consistency for the CISS was calculated using Cronbach alpha as follows: Task = 0.85, Emotion = 0.86, Avoidance = 0.83.

For the CISS: Population norms for men and women combined (N = 80).

Emotional coping mean = 13.76 (5.38)

In the present study, consistent with the literature on MS populations, Emotional coping at baseline was higher than normal population mean scores:

Biofeedback: Mean = 22.95 (6.79)

Control: Mean = 21.35 (6.33)

Task coping mean = 24.74 (4.74)

In the present study, Task coping at baseline was comparable to normal population mean scores:

Biofeedback: Mean = 24.45 (6.92)

Control: Mean = 24.75 (7.21)

Depression, Anxiety, Stress Scale

The DASS[24] is a 42-item self-report questionnaire. It provides Australian normative data and has high reliability for measuring the existence of stress, anxiety, and depression in a self-report format, based on the person's previous week.

The DASS was designed to measure three negative affective states: depression, anxiety, and stress. The depression scale measures hopelessness, lack of interest in activities, anhedonia, and inertia. The anxiety scale measures skeletal musculature effects, situational anxiety, and autonomic arousal. The stress scale measures difficulty relaxing, hyperarousal, and nervous energy. Cronbach alpha coefficients for the three 14-item DASS scales are as follows: Depression = 0.91, Anxiety = 0.84, and Stress = 0.90 (N = 2914).[24] The tripartite model of stress, anxiety, and depression shows good convergent validity with the Beck Anxiety Inventory (BAI). Cronbach alpha coefficients for the DASS (stress and anxiety) correlate with the BAI: 0.64 for stress and 0.81 for anxiety.

Cronbach alpha coefficients calculated for the three DASS items in the present study were as follows: Depression = 0.89, Anxiety = 0.86, and Stress = 0.81.

Fatigue Severity Scale

The Fatigue Severity Scale (FSS) is a 9-item self-report questionnaire. Participants rate their answers on a scale of 1 to 7. By convention, the total score is divided by 9. Scores of 4 or greater are considered clinically "severe" and scores less than 4 are considered clinically "mild" according to the developer's mean cutoff.[28] The FSS has been found to be stable over test-retest conditions for populations of people living with MS,[23] and has been used to differentiate fatigue from clinical depression with a Cronbach alpha of 0.81.[23] Internal consistency in the present study for the FSS was calculated using the Cronbach alpha = 0.91.

Supplementary Appendix 3. **Procedures**

Mindful Breathing Awareness Procedure

"Place your left hand over your mid-lower sternum and your right hand over your belly. Breathe normally and observe where your hands are moving.

"When you breathe using your chest, there is only a limited amount of movement that your ribs and intercostal muscles allow. This movement causes pockets of space with negative pressure (pleural spaces) that then draw air in. However, when you use your diaphragm, the smooth muscle just below the bottom of your rib cage, it draws down and the belly moves out, creating a large space of negative pressure, allowing much more air to be drawn in to the bottom of your lungs.

"Breathing rapidly, because of activation of the flight/fight response, heart rate increases and muscle tension increases. It sends a message back to your brain to keep sending adrenaline to help you cope with whatever the threat is."

Attach the patient to the machine:

Place the Velcro waist band around the patient's waist, with the small box component at the level of the belly button, tight enough to keep some tension but loose enough to still be comfortable when the patient breathes out. Ensure that the band is not twisted. Ensure that the wire is firmly attached and place the end of the wire into the encoder box at input "G."

The following script was followed for the mindful breathing awareness exercise.

"Please hold your belly as if it was a large balloon." Ask them to simplify breathing. "Breathe as if you were filling up the balloon. When you breathe out, the balloon contracts."

Recommend that they try breathing in for a count of 3 seconds, and then out for 3 seconds, to achieve 10 breaths per minute. Give them 120 seconds to practice.

Biofeedback only: “At the blue line, we see a wavelike pattern that should be created (6–12 breaths per minute is desirable in relaxed breathing). We see a windmill in the right-hand side of the screen that is set to turn when your breath has a depth or amplitude at the diaphragm of 3.” Write down these parameters for the patient to remember during the session. As the participant begins to practice, observe the changes that this causes to the wavelike pattern on the screen and point this out to the participant.

Progressive Muscle Relaxation Procedure

The following script was read out to introduce progressive muscle relaxation (PMR) to each participant:

“Progressive muscle relaxation allows you to identify muscles that you may be contracting without realizing that you are. Under my instruction, you are going to squeeze muscles one at a time as you breathe in and then release them as you breathe out. This allows you to identify tight muscles and release your tension. Squeezing muscles also releases endorphins, which relax muscles. We start with your eye muscles, and move progressively down through muscle groups in your jaw, shoulders, core, arms, legs and feet.”

Biofeedback only:

“This green jumpy line demonstrates the total muscle activity of the muscle on which the electrodes are sitting, that is the summation of the action potentials sent by the motor nerve there. The more jumpy the line, the greater the activation. The higher the line is up the scale, the greater the total activation or tensions your muscle is holding. We are aiming for a total tension

reading to be reduced (lower than 4 µV is relaxed), and get the line to be less jumpy (more control). Please note that the scale on the line graph will change to fit your activity, so if you activate the muscle, your response will be recorded on a larger scale and the scale will take one screen to zoom in again on your response. The bar graph shows your average muscle tension every 20 seconds and allows you to see how you are going over the course of the session."

Supplementary Appendix 4. **Session outline**

Week 1	**Week 2**	**Week 3**	**Follow-up**
biofeedback	**biofeedback**	**biofeedback**	**biofeedback**

Attend biofeedback session, connected to machine. Encouraged to use the screens to see changes in breathing rate and muscle tension during session. Progressive muscle relaxation, education about flight/fight response and mindful breathing. Complete DASS, CISS, and FSS. Encouraged to practice the breathing and PMR for 5 minutes twice daily and make a note of this activity in a diary.	Attend biofeedback session, connected to machine. Encouraged to use the screens to see changes in breathing rate and muscle tension during session. Progressive muscle relaxation, education about flight/fight response and mindful breathing. Complete DASS, CISS, and FSS. Encouraged to practice the breathing and PMR for 5 minutes twice daily and make a note of this activity in a diary.	Attend biofeedback session, connected to machine. Encouraged to use the screens to see changes in breathing rate and muscle tension during session. Progressive muscle relaxation, education about flight/fight response and mindful breathing. Complete DASS, CISS, and FSS, ask whether intervention made a difference. Encouraged to continue to practice the breathing and PMR for 5 minutes twice daily and make a note of this activity in a diary.	DASS, FSS, and CISS posted with self-addressed stamped envelope.

Week 1	Week 2	Week 3	Follow-up
control	control	control	control

Attend session, connected to machine. Progressive muscle relaxation, education about flight/fight response and mindful breathing. Complete DASS, CISS, and FSS. Encouraged to practice the breathing and PMR for 5 minutes twice daily and make a note of this activity in a diary.	Attend session, connected to machine. Progressive muscle relaxation, education about flight/fight response and mindful breathing. Complete DASS, CISS, and FSS. Encouraged to practice the breathing and PMR for 5 minutes twice daily and make a note of this activity in a diary.	Attend session, connected to machine. Progressive muscle relaxation, education about flight/fight response and mindful breathing. Ask about whether intervention made a difference. Complete DASS, CISS, and FSS. Encouraged to continue to practice the breathing and PMR for 5 minutes twice daily and make a note of this activity in a diary.	DASS, FSS, and CISS posted with self-addressed stamped envelope.